UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF WISCONSIN

PROMEGA CORPORATION, ET AL. Plaintiff, vs. LIFE TECHNOLOGIES CORPORATION, INVITROGEN IP HOLDINGS, INC., AND APPLIED BIOSYSTEMS, LLC, Defendants.	Civil Action No. 10-CV-281

DEFENDANTS' MEMORANDUM IN SUPPORT OF MOTION REQUESTING CLAIM CONSTRUCTION

Defendants Life Technologies Corporation, Invitrogen IP Holdings, Inc., and Applied Biosystems, LLC (collectively, "Defendants") submit this Memorandum in Support of their Motion Requesting Claim Construction.

I. INTRODUCTION

Defendants set forth herein seven claim terms and proposed constructions identified by Defendants in conjunction with the Court's Preliminary Pretrial Conference Order, Docket #69, as amended. Promega did not identify any claim terms or proposed constructions on the date set by the Court (February 28, 2011), or even as of the time this brief was filed.[1]

The asserted Promega patents[2] generally concern methods and kits for using human DNA as a "fingerprint." This is useful, for example, in distinguishing one individual from another in a

[1] As Promega has been advised, Defendants reserve the right to amend or supplement their proposed constructions once Promega provides detailed infringement contentions to Defendants (to date, Promega has not done so despite Defendants' discovery requests and subsequent follow-up).

[2] U.S. Patent Nos. 5,843,660 ("the '660 patent"); 6,221,598 ("the '598 patent"); 6,479,235 ("the '235 patent"); and 7,008,771 ("the '771 patent"). The Promega patents are a family of patents all relating back to U.S. Application

criminal investigation, as dramatized in popular television series such as "CSI." The Promega patents use so-called multiplex amplification reactions of short tandem repeat (STR) loci found in human DNA to generate such a fingerprint. Because the lengths of STR loci vary highly from individual to individual, it is possible to compare the STR "fingerprint" or profile of one individual or source against known profiles in order to determine identity or a match.

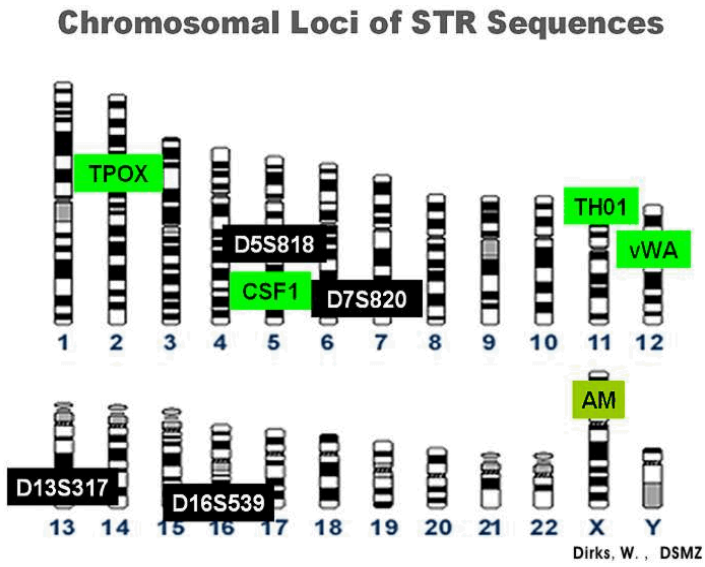
The purported inventions of the Promega patents are at best minor and incremental improvements over the prior art and give rise, therefore, to claims which are narrow in scope. The general concept of using DNA as a fingerprint was known in the prior art. It was further known that so-called multiplex amplification reactions of STR loci could be used to generate such a fingerprint. The intrinsic evidence—the specifications and prosecution histories of the Promega patents—shows that the inventors' goals were modest improvements over this art, *i.e.*, merely identifying particular sets of STR loci that would work together in a multiplex amplification reaction. This was because, as the intrinsic evidence shows, skilled artisans had not managed to hone the relevant technology down to a science or an art; it remained from the parent application of the Promega patents through the filing date of the latest of the Promega patents an arduous trial-and-error proposition. A multitude of experimental parameters, laborious screening, inexplicable and unpredictable results, and an inability to predict success were the well-documented norm. A claim construction properly aligning the scope of the claims to the scope of the alleged inventions is therefore necessary.[3]

Serial No. 08/316544 ("the '544 parent application"), which was ultimately abandoned. The '660 patent is a continuation-in-part of the '544 parent application. The '598 patent is a continuation of the '544 parent application. The '235 is a continuation-in-part of the '660 patent, and the '771 patent is a division of the '235 patent. Promega also asserts infringement of U.S. Patent No. RE37984, but neither Defendants nor Promega identified any claim terms from this patent for construction.

[3] In 2002, this Court construed various claims from the '660 and '598 patents in the case of Promega Corp. v. Applera Corp. *et al*. (No. 01-C-244-C). The Court's claim construction orders from that case are appended as Exhibits 16 and 17 to the Sun Declaration filed concurrently herewith.

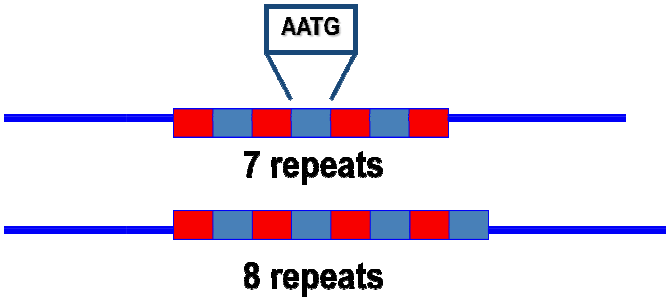
II. THE RELEVANT TECHNOLOGY AND THE PROMEGA PATENTS

The technology at issue involves the simultaneous amplification of multiple short tandem repeat (STR) loci from one or more DNA samples. An STR locus is a region of DNA which contains repeats of a particular nucleotide sequence. Declaration of Amy Sun in Support of Defendants' Motion Requesting Claim Construction ("Sun Decl."), Ex. 6 ('660 patent), col. 1, ll. 35-37; Sun Decl., Ex. 7 ('598 patent), col. 1, ll. 32-33. For example, the DNA sequence ATT (adenine-thymine-thymine) may be repeated ten times in tandem (*i.e.* in a row) at a particular locus. The DNA sequence GAAG (guanine-adenine-adenine-guanine) may be repeated twelve times in tandem at another STR locus. The figure below shows the locations of STR loci such as TPOX, D5S818, and CSF1 on the chromosomes of the human genome.



The number of repeats of a given sequence at a particular STR locus varies highly from individual to individual. As described in the Promega patents, "[s]uch length and/or sequence variation is referred to as 'polymorphism.' Any region (i.e. 'locus') of DNA in which such a variation occurs is referred to as a 'polymorphic locus.'" Sun Decl., Ex. 8 ('235 patent), col. 1, ll. 42-25; Sun Decl., Ex. 9 ('771 patent), col. 1, ll. 47-50. For example, one individual's DNA may

have eleven CCCG (cytosine-cytosine-cytosine-guanine) repeats at a given STR locus, while another individual may have fourteen at the same locus. Each of these variations is referred to as an "allele" (or "marker") of the particular locus. Sun Decl., Ex. 6 ('660 patent), col. 1, ll. 47-50. Further, each individual has two alleles for every STR locus, one inherited maternally and the other paternally. As shown in the figure below, the AATG (adenine-adenine-thymine-guanine) sequence may be repeated seven times in one allele and eight times in the other allele at the STR locus of a particular individual. All of this was known in the prior art. Id. cols. 1-2.

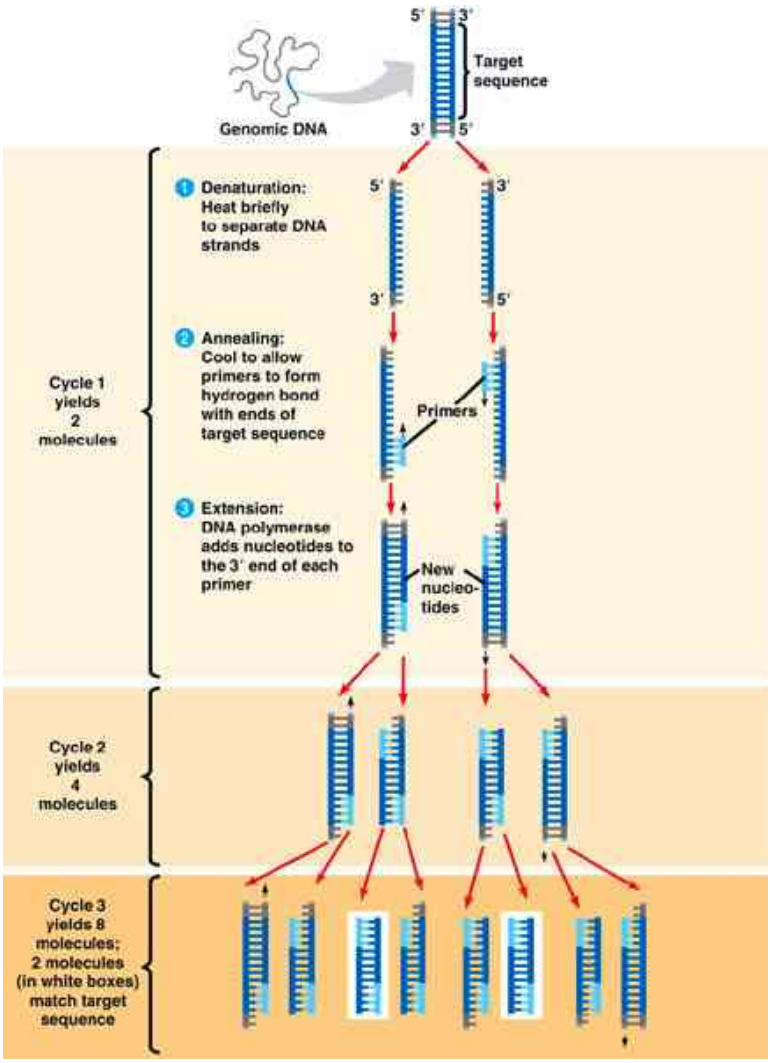


Determining the unique set of alleles at multiple loci in an individual's DNA gives rise to an STR profile or fingerprint unique to the individual. This method is known as STR profiling and can serve as the basis for identifying individuals, determining whether two samples are a match or originate from two individuals, determining whether one sample contains a mixture of two individuals' DNA, etc. Consequently, STR profiling is useful in the fields of "forensic analysis, paternity determination, monitoring of bone marrow transplantation, linkage mapping, and detection of genetic diseases and cancers." Sun Decl., Ex. 6 ('660 patent), col. 8, ll. 2-4; Sun Decl., Ex. 8 ('235 patent), col. 1, ll. 28-45; Sun Decl., Ex. 9 ('771 patent), col. 1, ll. 33-50. All of this was known in the prior art. Sun Decl., Ex. 6 ('660 patent), col. 8; Sun Decl., Ex. 8 ('235 patent), cols. 3-4; Sun Decl., Ex. 9 ('771 patent), cols. 3-4.

When performing STR analysis, it is necessary to amplify (make copies of) the STR loci of interest in order to obtain a detectable amount for analysis. For reasons of efficiency, it is

advantageous to co-amplify multiple loci in a single reaction rather than individually. Sun Decl., Ex. 6 ('660 patent), col. 2, ll. 13-17 ("To minimize labor, materials and analysis time, it is desirable to analyze multiple loci and/or more samples simultaneously. One approach for reaching this goal involves amplification of multiple loci simultaneously in a single reaction."); Sun Decl., Ex.7 ('598 patent), col. 1, ll. 56-60; Sun Decl., Ex. 8 ('235 patent), col. 3, ll. 3-5; Sun Decl., Ex. 9 ('771 patent), col. 8-10. Amplification of STR loci is most commonly carried out by the polymerase chain reaction (PCR). A short video tutorial of PCR amplification of STR loci and subsequent analysis using capillary electrophoresis can be found at: http://www.youtube.com/user/dnacenter#p/u/3/PgrAc7WMDTY and http://www.youtube.com/user/dnacenter#p/u/2/JZtAsqGWD6c.

As shown in the figure below, the basic idea of PCR is to (1) separate double-stranded DNA into single strands, (2) allow primers (initiators of DNA synthesis) which specifically target the desired STR loci to bind to the single strands at the target loci, (3) replicate the single strands beginning at these primer sites into double-stranded DNA again, and (4) repeat the process until a sufficient amount of copies of the desired STR loci is generated. In multiplex PCR amplification reactions, multiple STR loci are simultaneously targeted and multiple corresponding primers are used simultaneously in a single reaction.



According to the disclosure of Promega patents, "[s]uch 'multiplex' amplifications, as they are called, have been described ***extensively*** in the literature," even at the time the earliest two of the Promega patents were filed. Sun Decl., Ex. 6 ('660 patent), col. 2, ll 17-18 (emphasis added); Sun Decl., Ex. 7 ('598 patent), col. 1, ll. 60-61 (emphasis added). By that time, for example, "[m]ultiplex amplification sets ha[d] been ***extensively developed*** for analysis of genes related to human genetic diseases such as Duchenne Muscular Distrophy . . . Lesch-Nyhan Syndrome . . . Cystic Fibrosis . . . and Retinoblastoma." Sun Decl., Ex. 6 ('660 patent), col. 2, l. 19 – col. 3, l. 13 (emphasis added); Sun Decl., Ex. 7 ('598 patent), col. 1, l. 61 – col. 2, l. 2

(emphasis added). Therefore, the concept and technology of multiplexing was not in any way new by the time Promega sought to patent its claimed inventions.

Moreover, the specifications of the Promega patents explain that multiplexes of large numbers of loci (*e.g.*, a "highly discriminating octoplex" and even multiplexes of 11 STR loci) had already been described in the prior art. Sun Decl., Ex. 6 ('660 patent), col. 3, l. 10; *see also* Sun Decl., Ex. 8 ('235 patent), col. 3, ll. 7-8; Sun Decl., Ex. 9 ('771 patent), col. 3, ll. 12-13. Multiplexing specific STR loci was also already known in the art, including the specific STR loci claimed in the Promega patents. Sun Decl., Ex. 6 ('660 patent), col. 3, ll. 46-47 ("[T]here are multiplex amplification procedures for specific loci . . . ."); Sun Decl., Ex. 7 ('598 patent), col. 2, ll. 37-38.[4] Finally, several of the primers in the Promega patents were also already known in the art.[5]

What scientists had not yet managed to discover was a consistent and predictable way to multiplex any arbitrary set of STR loci. For example, the loci in a given set may simply fail to amplify in a multiplex environment, even though they amplify individually without issue. Sun Decl., Ex. 1 at 324. Additionally, amplification may occur at sites on the DNA other than the target STR locus. Id. The loci in the multiplex may also amplify at unequal levels. Sun Decl., Ex. 4 at 248. The primers may bind to each other (primer-dimer formation) rather than their target STR loci. Sun Decl., Ex. 1 at 324. The alleles of different STR loci may overlap, making it impossible to determine the alleles present at each of the individual loci. Id. Enzyme slippage during amplification may cause "stutter" banding, again making it impossible to definitively

[4] As just one example, one of the prior art references raised during prosecution of the Promega patents disclosed a multiplex of four STR loci known as HUMFESFPS, HUMTH01, HUMF13A01, and HUMVWFA31. Sun Decl., Ex. 2 at 242. All of these loci are recited in various claims of the Promega patents. *See generally* Sun Decl., Ex. 6 ('660 patent), cols. 63-70; Sun Decl., Ex. 7 ('598 patent), cols. 35-42; Sun Decl., Ex. 8 ('235 patent), cols. 57-62; Sun Decl., Ex. 9 ('771 patent), cols. 59-62.

[5] Again, as just one example, another prior art reference raised during prosecution of the Promega patents disclosed "primers identical to the primers of SEQ ID NO: 1, 2, 9, 15, 16, 19, 20, 27, 28, and 30." Sun Decl., Ex. 3 at 105.

assign alleles to a particular STR locus. Sun Decl., Ex. 2 at 180 (¶¶ 19, 22). Anomalous and inexplicable bands may appear when attempting to visualize alleles of the amplified STR loci on a gel. Id. The list is by no means exhaustive.

In sum, while the concept and technology of multiplex amplification reactions were not new, many difficulties existed in the art. The claimed novelty of Promega's patents was therefore the narrow discovery of successful methods and materials for multiplexing certain specific sets or groups of STR loci. As acknowledged in the specifications of the Promega patents, "[w]hile there are [already] multiplex amplification procedures for ***specific loci***, the use of multiplex amplification procedures is greatly desired for the detection of alleles in ***other types of loci such as specific STR loci***." Sun Decl., Ex. 6 ('660 patent), col. 3, ll. 46-49 (emphasis added); *see also* Sun Decl., Ex. 7 ('598 patent), col. 2, ll. 37-40; Sun Decl., Ex. 8 ('235 patent), col. 4, ll. 5-8; Sun Decl., Ex. 9 ('771 patent), col. 4, ll. 9-13. Promega claimed to have discovered successful methods and materials for multiplexing such other specific sets of STR loci, summarizing its invention as follows:

> It is, therefore, an object of the present invention to provide a method and materials for the simultaneous amplification of multiple distinct polymorphic short tandem repeat (STR) loci using PCR or other amplification systems to determine, in one reaction, the alleles of each locus contained within the multiplex. Multiplex analysis of ***the sets of specific STR loci disclosed herein have not been previously described*** in the prior art.

Sun Decl., Ex. 6 ('660 patent), col. 3, ll. 54-61 (emphasis added); *see also* Sun Decl., Ex. 7 ('598 patent), col. 2, ll. 43-49; Sun Decl., Ex. 8 ('235 patent), col. 4, ll. 22-32; Sun Decl., Ex. 9 ('771 patent), col. 4, ll. 27-37.

III. THE LAW OF CLAIM CONSTRUCTION

Claim construction is a legal determination to be made by the Court. Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996); Markman v. Westview Instruments,

Inc., 52 F.3d 967, 979 (Fed. Cir. 1995) (*en banc*), *aff'd*, 517 U.S. 370 (1996). In construing the claims, the Court looks first to the intrinsic evidence: the claims, specification, and prosecution history. Teleflex, Inc. v. Ficosa N. Am. Corp., 299 F.3d 1313, 1324-25 (Fed. Cir. 2002).

Claims are generally given their "ordinary and customary" meaning "in the context of the particular claim" and "the context of the entire patent" as a whole, as understood by a person of ordinary skill in the art when the patent application was filed. Phillips v. AWH Corp., 415 F.3d 1303, 1312-13 (Fed. Cir. 2005); ACTV, Inc. v. Walt Disney Co., 346 F.3d 1082, 1088 (Fed. Cir. 2003). The specification "is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." Phillips, 415 at 1315 (quoting Vitronics, 90 F.3d at 1582). The prosecution history also "may affect the scope of the invention." Vitronics, 90 F.3d at 1582. It "can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it otherwise would be." Phillips, 415 F.3d at 1318 (citing Vitronics, 90 F.3d at 1582-83).

Lastly, after considering the intrinsic evidence, the Court may look to extrinsic evidence, such as dictionaries and expert testimony, to "shed useful light on relevant art." Phillips, 415 F.3d at 1317.

Where, as here, multiple patents "derive from the same initial application, the prosecution history regarding a claim limitation in any patent that has issued applies with equal force to subsequently issued patents that contain the same claim limitation." Elkay Mfg. Co. v. Ebco Mfg. Co., 192 F.3d 973, 980 (Fed. Cir. 1999); *see also* Advanced Cardiovascular Sys. v. Medtronic, 265 F.3d 1294, 1305 (Fed. Cir. 2001) ("The prosecution history of a related patent can be relevant if, for example, it addresses a limitation in common with the patent in suit.").

IV. CLAIM CONSTRUCTIONS

A. "a set of . . . loci"

Proposed Construction: a collection of only the loci listed in the claim

Construction of this term is necessary to resolve a disputed issue concerning infringement. Under the proposed construction above, the accused products do not infringe the asserted claims of the Promega patents because they amplify sets of loci other than the sets of loci recited in the asserted claims.

i. The Uncertain Technological Landscape Means that Promega's Actual (Alleged) Inventions Are Limited to the Sets of Loci Listed in the Claims

During prosecution, the claims of the Promega patents were subjected to repeated rejection based on examples of successful multiplex reactions already taught in the prior art. In fact, in Promega's own words, multiplexing had already been "described extensively" and "extensively developed" by the time it submitted patent applications for its claimed inventions. Sun Decl., Ex. 6 ('660 patent), col. 1, ll. 18-19; *see also* Sun Decl., Ex. 7 ('598 patent), col. 1, ll. 61-62. Large multiplexes of eight and even eleven STR loci had already been demonstrated. Sun Decl., Ex. 6 ('660 patent), col. 3, l. 10; *see also* Sun Decl., Ex. 8 ('235 patent), col. 3, ll. 7-8; Sun Decl., Ex. 9 ('771 patent), col. 3, ll. 12-13.

Promega's argument to overcome the prior art was therefore that designing and successfully carrying out a multiplex reaction was an unpredictable, labor-intensive process involving extensive trial and error and adjustment of numerous possible reaction parameters. As such, no relationship could be drawn between one successful multiplex reaction, *i.e.*, the prior art, and another, *i.e.*, the multiplex reactions disclosed in the Promega patents. Below are just a few of the statements Promega made during prosecution of the Promega patents, including not only attorney arguments but sworn statements by co-inventor Cynthia J. Sprecher:

> [T]he process of identifying sets of loci which can be amplified and analyzed together is an unpredictable one, requiring a considerable amount of experimentation, even with the guidance of references . . . .
>
> "Therefore, given the unpredictable nature of multiplex STR loci set selection at the time the present invention was made, the results were unpredictable, and screening was required to ensure ***any*** given set of STR loci could be amplified and evaluated together."
>
> "STR loci selection and co-amplification was shown to be a non-trivial matter and that success in these endeavors was by no means expected."

Sun Decl., Ex. 3 at 177 (Sprecher Declaration) (emphasis added); Sun Decl., Ex. 4 at 247 (Sprecher Declaration) (emphasis added), 249 (emphasis added), 253 (emphasis added).

Due to the abundance and pervasiveness of such remarks in the prosecution histories, only a selection has been reproduced here. A comprehensive aggregation is found in Appendix A, hereby fully incorporated by reference.

Expert opinions are in accord regarding the unpredictable state of the art. In a previous litigation before this Court between Promega and Applera Corporation (predecessor to Defendant Applied Biosystems, LLC) (No. 01-C-244-C), the experts on both sides of the case provided consistent opinions regarding the unpredictability of multiplexing technology during the relevant time period. Professor Richard Gibbs, expert witness for Applera Corporation, explained:

> [O]ne of skill in the art would not know, absent a specific pre-existing teaching, whether a given multiplex would successfully co-amplify until the co-amplification reaction was attempted and successfully performed.
>
> . . .

> In fact, the process of creating a multiplex becomes more complicated with the addition of each new STR loci [sic] to the multiplex, such that the addition of the 8th loci [sic] to a 7-plex is more complicated than the addition of the 7th loci [sic] to a 6-plex, and so on.

Sun Decl., Ex. 10 at 17-18 (emphasis added).

Promega's expert witness, Randall L. Dimond, its own Vice President and Chief Technical Officer, agreed:

> In contemplating a new multiplex one cannot predict with any reasonable degree of certainty that any particular set of conditions will be successful. One can only hope that through arduous optimization of a multitude of parameters a solution can be found. In fact, in many cases this process still leads only to failure.

Sun Decl., Ex. 11, ¶ 90 (emphasis added); *see also* id. ¶¶ 66,99; Sun Decl., Ex. 15, Attachment 2 (Curriculum Vitae of Randall L. Dimond).

The intrinsic and extrinsic evidence uniformly depict an unpredictable and failure-ridden state of the art. Given this context, by Promega's own admission it simply cannot be said that it invented multiplexes with open-ended sets of STR loci. Renishaw PLC v. Marposs Società per Azioni, 158 F.3d 1243, 1250 (Fed. Cir. 1998) (explaining that "the interpretation to be given a term can only be determined and confirmed with a full understanding of what the inventors ***actually invented***") (citing Markman v. Westview Instruments, Inc., 517 U.S. 370, 389 (1996)) (emphasis added); *see also* Phillips, 415 F.3d at 1321 ("The patent system is based on the proposition that the claims cover ***only the invented subject matter***.") (emphasis added).

Rather, at most Promega can be said to have discovered (if anything at all) ways to multiplex specific closed sets of STR loci, *i.e.*, those sets disclosed in the examples in the specifications of the Promega patents and later explicitly listed in the claims. *See* Capon v. Eshhar, 418 F.3d 1349, 1358 (Fed. Cir. 2005) ("It is well recognized that in the 'unpredictable' fields of science, it is appropriate to recognize the variability in the science in determining the

scope of the coverage to which the inventor is entitled.") To add even a single additional locus to one of these sets of loci and attempt to multiplex the new set would, in Promega's own words, invite "a considerable amount of experimentation" with a "myriad of parameters," "laborious screening," "inexplicable" and "unpredictable" results, and "success [that] by no means [was] expected." Sun Decl., Ex. 3 at 177. (Sprecher Declaration); Sun Decl., Ex. 4 at 247; Sun Decl., Ex. 1 at 302; Sun Decl., Ex. 4 at 251; Sun Decl., Ex. 1 at 274; Sun Decl., Ex. 4 at 253.

The reasoning Promega used to overcome the prior art must apply with equal force to Promega's own alleged inventions. If based on the unpredictability of the art the sets of loci Promega multiplexed were inventive over or beyond the scope of prior art multiplexes using different sets of loci, then multiplexes containing loci outside Promega's multiplex sets are also beyond the scope of Promega's claimed inventions. Capon, 418 F.3d at 1358. The proper scope of the term "a set of . . . loci" is therefore, as Defendants propose, limited to the specific loci listed in the claims. Id.

ii. The Examiner's Understanding and Promega's Own Characterization of the Alleged Inventions are Narrow

Indeed, such a construction accords with Promega's explicit characterization of its alleged inventions. In particular, Promega did not claim to have invented general methods and/or materials which solved the problems in the prior art and enabled consistent and predictable multiplex reactions. Instead, over and over Promega argued that it was the *specific "sets," "groups," or "combinations" of loci listed in the claims* that were novel and nonobvious over the prior art.

In the Summary of the Invention for each and every one of the Promega patents, Promega asserts: "Multiplex analysis of the ***sets of loci disclosed herein*** has not been previously described in the prior art." Sun Decl., Ex. 9 ('771 patent), col. 4, ll. 35-37; Sun Decl., Ex. 8 ('235 patent),

col. 4, ll. 30-32; Sun Decl., Ex. 7 ('598 patent), col. 2, ll. 47-49; Sun Decl., Ex. 6 ('660 patent), col. 12, ll. 39-40. *See* Praxair, Inc. v. ATMI, Inc., 543 F.3d 1306, 1324 (Fed. Cir. 2008) ("The claims of the patent must be read in light of the specification's consistent emphasis on this fundamental feature of the invention."); C.R. Bard, Inc. v. U.S. Surgical Corp., 388 F.3d 858, 864 (Fed. Cir. 2004) ("Statements that describe the invention as a whole, rather than statements that describe only preferred embodiments, are more likely to support a limiting definition of a claim term.") (citation omitted). *See also* Sun Decl., Ex. 9 ('771 patent), col. 9, ll. 10-12 ("The specific combinations of loci described herein are unique to this application."); Sun Decl., Ex. 8 ('235 patent), col. 8, l. 66 – col. 9, l. 1.

In addition, during prosecution Promega repeatedly made similar such statements:

> [T]he present invention enable[s] skilled artisans to co-amplify and analyze sets of loci not heretofore identified and disclosed as suitable for such analysis.
>
> The combined references do not disclose or even suggest the presently claimed combinations of loci, per se, and the references clearly do not disclose or suggest that any arbitrary combination of loci can be co-amplified without undue experimentation.

Sun Decl., Ex. 2 at 227 (emphasis added); Sun Decl., Ex. 1 at 304 (emphasis added).

Again, because such statements are found pervasively in the prosecution histories of the Promega patents, only a limited number have been reproduced here. Appendix B contains a comprehensive aggregation and is hereby fully incorporated by reference.

The clear theme that emerges from the prosecution histories is that what Promega "actually invented" (if anything) were materials and methods which were found to be successful in amplifying particular closed sets of STR loci, *i.e.*, those sets of loci specifically listed in the claims. Renishaw, 158 F.3d at 1250 ("[T]he interpretation to be given a term can only be

determined and confirmed with a full understanding of what the inventors ***actually invented*** . . . .") (emphasis added); Phillips, 415 F.3d at 1321.

Indeed, it was also the examiner's understanding that the alleged inventiveness of the Promega patents derived from the specific sets of loci listed in the claims. When the examiner issued a notice of allowance for the '598 patent, she explained in her statement of reasons for allowance:

> [T]he art does not teach the ***specific combinations provided in the claims***. Furthermore, as found in the declaration submitted by Cynthia Sprecher, unexpected results were obtained. While all of the ***instant STR loci were known*** in the art at the time the invention was made, the ***combinations of STR loci of the instant claims*** for use in multiplex amplification and [sic] was ***not contemplated***. . . . Therefore . . . the instant claims are allowable.

Sun Decl., Ex. 3 at 239 (emphasis added). The examiner did not make a finding that Promega's alleged inventions were particularly far-reaching or pioneering. In fact, the STR loci which were the subject of Promega's claims "were known." Id. Rather, it was the examiner's understanding that Promega's inventions were defined by the "specific combinations [of loci] provided in the claims." Id. The proper construction for the term "a set of . . . loci" is therefore "a collection of only the loci listed in the claim."

iii. The Written Descriptions of the Alleged Inventions in the Specifications Confirm the Narrow Scope of the Claims

The written descriptions of the Promega patents provide further confirmation that what Promega actually (allegedly) invented is limited to the sets of loci listed in the claims. *See* Reiffin v. Microsoft Corp., 214 F.3d 1342, 1345-46 (Fed. Cir. 2000) ("[T]he purpose of the written description requirement is to ensure that the scope of the right to exclude . . . does not overreach the scope of the inventor's contribution to the field of art ***as described in the patent specification***.") (emphasis added) (citation and internal quotations omitted); Capon, 418 F.3d at

1357 ("[A] patent must describe the technology that is sought to be patented; the requirement serves . . . to demonstrate that the patentee was in ***possession of the invention that is claimed***.") (emphasis added); Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 928 (Fed. Cir. 2004) (emphasizing that the specification must "set forth enough detail to allow a person of ordinary skill in the art to understand what is claimed and to recognize that the inventor ***invented what is claimed***") (emphasis added). Therefore, the Federal Circuit has instructed:

> It is well recognized that in the "unpredictable" fields of science, it is appropriate to recognize the variability in the science in determining the scope of the coverage to which the inventor is entitled. Such a decision usually focuses on the ***exemplification in the specification***.

Capon, 418 F.3d at 1358 (emphasis added).

Turning to the examples in the specifications of the Promega patents, therefore, the vast disconnect between the actual (alleged) invention and a broad construction of the claims becomes even more apparent. The '598 patent provides examples of multiplex reactions involving sets of only 2 to 4 loci. Sun Decl., Ex. 7 ('598 patent) at cols. 11-22. Moreover, these multiplex sets are made up of combinations of only 17 specific STR loci. Id. Yet according to the '598 patent, "[i]t is estimated that there are 2,000,000 expected trimeric and tetrameric STRs present as frequently as once every 15 kilobases in the human genome." Sun Decl., Ex. 7 ('598 patent) at col. 1, ll. 33-35 (citation omitted); *see also* Sun Decl., Ex. 6 ('660 patent), col. 1 at ll. 37-39. When including pentameric, hexameric, and heptameric STRs in the count, the already large 2 million figure is even larger. *See* id. at col. 1, ll. 32-33 ("STR loci consist of short, repetitive sequence elements of 3 to 7 base pairs in length."). As Promega itself argued to the examiner:

> Considering how many possible combinations there are of tri-, tetra-, and pentanucleotide STR loci in the human genome, and considering the anomalous band problems observed by Kimpton *et*

> *al*. '93 with the multiplex sets disclosed therein, Applicants respectfully submit that Kimpton *et al*. '93, even when viewed in combination with Caskey *et al*. and Kimpton *et al*. '94, does not teach or suggest the present claimed invention."

Sun Decl., Ex. 3 at 160.

Any broader construction would therefore pose the question, whether based on the examples in the specification of the '598 patent, which disclose multiplex sets of 2 to 4 loci selected from a pool of 17 loci, in an admittedly uncertain state of the art, Promega was "in possession" of multiplex sets of unlimited size using loci drawn from a pool of in excess of 2,000,000 possible STR loci. Capon, 418 F.3d at 1357. The answer could only be no. Id.; *see also* LizardTech, Inc. v. Earth Res. Mapping, Inc., 424 F.3d 1336, 1346 (Fed. Cir. 2005) ("[T]he description of one method for creating a seamless DWT does not entitle the inventor of the '835 patent to claim ***any and all means*** for achieving that objective.") (emphasis added). In fact, in the Summary of the Invention for the '598 patent, Promega asserts: "[T]he present invention is directed to a method of simultaneously analyzing multiple STR sequences ***in the following groups of loci***," thereafter reciting closed groups of between two to four loci. Sun Decl., Ex. 7 ('598 patent), col. 3, ll. 4-34 (emphasis added). A broad construction would therefore "overreach" the scope of the alleged invention "as described in the patent specification." Reiffin, 214 F.3d at 1345-46.

The same is true with respect to the '660, '235, and '771 patents. The examples in the specification of the '660 patent involve multiplexes of between 3 and 8 loci selected from a pool of 27 loci. The examples in the specifications of the '235 and '771 patents both involve multiplexes of either 13 or 16 loci selected from a pool of 34 loci. In light of the foregoing, the only proper construction for the term "a set of . . . loci" is a collection of only the loci listed in the claims.

iv. The Term "Comprising" in the Claims Does Not Abrogate Explicit Claim Limitations

The term "a set of . . . loci" is not open-ended, notwithstanding the use of the transition phrase "comprising" in the claims. While the term "comprising" may signify that the recited elements of a claim are "nonexclusive," it "does not reach into [and] render every word and phrase" within the individual claim elements open-ended. Dippin' Dots, Inc. v. Mosey, 476 F.3d 1337, 1343 (Fed. Cir. 2007). *See also* Sandisk Corp. v. Kingston Tech. Co., Inc., No. 10-cv-243-bbc, 2011 U.S. Dist. LEXIS 27696, at *59 (W.D. Wis. Mar. 15, 2011) ("The rule does not mean steps already present described in the claim can be broadened; it means only that an accused product may perform additional steps *not* claimed."). In other words, it is the claim which is (presumptively) open-ended with respect to claim elements, not the claim elements themselves. Infringement of a "comprising" claim is not avoided if a device includes elements beyond the recited claim elements. Dippin' Dots, 476 F.3d at 1343. Infringement is avoided, however, if each individual claim element "as recited" is not satisfied. Id. This merely reflects the fundamental principle that infringement must be proven on a claim-by-claim, element-by-element basis.

A "comprising" claim was asserted by the patentee in the Dippin' Dots case. The claim involved a "method of preparing and storing a free-flowing, frozen alimentary dairy product, comprising the steps of: (1) preparing an alimentary composition for freezing; (2) dripping said alimentary composition into a freezing chamber; (3) freezing said alimentary composition into beads; (4) storing said beads at a temperature at least as low as -20 degrees F. so as to maintain said beads free-flowing for an extended period of time; (5) bringing said beads to a temperature between substantially -10 degrees F. and -20 degrees F. prior to serving; and (6) serving said

beads for consumption at a temperature between substantially -10 degrees F. and -20 degrees F. so that said beads are free flowing when served." Dippin' Dots, 476 F.3d at 1340.

The district court had construed the term "beads" to mean "small frozen droplets . . . which have a smooth, spherical (round or ball shaped) appearance." Id. At 1342-43. "[I]rregular or odd shaped particles such as 'popcorn'" were excluded from the construction of "beads." Id. at 1343. The district court granted summary judgment of noninfringement because the accused processes produced both spherical and irregular shaped particles. Id.

On appeal, the patentee argued that the district court erred in its claim construction. Id. Based on the presence of the term "comprising" in the preamble of the claim, according to the patentee, the term "beads" should not have been limited to processes which produce only spherically shaped particles. Id. The Federal Circuit affirmed the district court's claim construction, reasoning:

> "Comprising" is not a weasel word with which to abrogate claim limitations. "Comprising" appears at the beginning of the claim – "comprising the steps of" – and indicates here that an infringing process could practice other steps in addition to the ones mentioned. Those six enumerated steps must, however, all be practiced ***as recited*** in the claim for a process to infringe. The presumption raised by the term "comprising" [*i.e.*, that the list of elements is nonexclusive] ***does not reach into each of the six steps to render every word and phrase therein open-ended*** . . . .

Id. (emphasis added) (citations and internal quotations omitted).

In Dippin' Dots, therefore, while the term "comprising" meant that the method steps of the claim were nonexclusive, the term "comprising" did not render the individual claim elements open-ended. A process could infringe the claim by performing additional steps beyond "freezing," "storing," and "serving" the "beads," but not by producing, freezing, storing, or serving anything other than "beads." The accused process, which failed to satisfy the individual "beads" claim element as recited, was held not to infringe.

The same principles are directly applicable to the claims presently at issue. The method claims of the Promega patents recite various steps for "selecting," "co-amplifying," and "evaluating" "a set of . . . loci." *See generally* Sun Decl., Ex. 6 ('660 patent), cols. 63-70; Sun Decl., Ex. 7 ('598 patent), cols. 35-42; Sun Decl., Ex. 8 ('235 patent), cols. 57-62; Sun Decl., Ex. 9 ('771 patent), cols. 59-62. The kit claims recite "primers" for co-amplifying "a set of . . . loci." Id. The term "comprising" is used throughout. Id.

What follows from Dippin' Dots is clear. The steps of the method and the contents of the kit are nonexclusive (presumptively). An infringing kit, for example, may contain additional components such as enzymes, buffers, and allelic ladders. *See*, *e.g.*, Sun Decl., Ex. 6 ('660 patent), col. 16, ll. 29-42; Sun Decl., Ex. 7 ('598 patent), col. 10, l. 61 – col. 11, l. 8; Sun Decl., Ex. 8 ('235 patent), col. 16, ll. 39-52; Sun Decl., Ex. 9 ('771 patent), col. 16, l. 57 – col. 17, l. 3. Likewise an infringing process may perform additional steps not claimed. However, the word "comprising" does not reach into individual claim elements, including the "a set of . . . loci" claim element, and render them open-ended. Dippin' Dots, 476 F.3d at 1343. Consequently, broadly construing the term "a set of . . . loci" as an open set is not justified. Id. The proposed construction "a collection of only the loci listed in the claim" respects the contours of the claims by ensuring that "comprising" is not operative upon the individual claim elements as recited. It is therefore the proper construction.

B. "gel"

Proposed Construction: a three-dimensional cross-linked network

Construction of this term is necessary to resolve a disputed issue concerning infringement. Under the proposed construction above, the accused products do not infringe the asserted claims of the Promega patents because they are not used in conjunction with a three-dimensional cross-linked network.

The claim term "gel" is not expressly defined or discussed in detail in the Promega patents. However, the prosecution histories show that a skilled artisan understood the term "gel" as a three-dimensional cross-linked network. Co-inventor James Schumm submitted a declaration during prosecution of the '660 patent, in which he stated: "[A] skilled artisan would have known that the principal tool used to separate amplified STR loci, polyacrylamide denaturing gel electrophoresis, is inherently limited in its capacity to resolve amplified DNA fragments . . . ." Sun Decl., Ex. 2 at 260, ¶ 7. Polyacrylamide gels are formed by the aggregation, or "polymerization," of acrylamide monomers through chemical cross-linking. *See* Sun Decl., Ex. 14 at 3 ("Polyacrylamide gel results from the polymerization of acrylamide monomer into long chains and the crosslinking of these by bifunctional compounds such as *N*,*N*′ – methylene bisacrylamide . . . reacting with free functional groups at chain termini."). Therefore, in the words of an inventor and skilled artisan, the "principal" gel used to separate STR loci was a three-dimensional cross-linked network. Sun Decl., Ex. 2 at 260, ¶ 7.

It is also acceptable to consult extrinsic evidence such as dictionaries and treatises to ascertain how a term was understood by persons skilled in the art. Phillips, 415 F.3d at 1317. The term "gel" is defined as "a three-dimensional cross-linked network" in the Dictionary of Polymers. Sun Decl., Ex. 12 at 208. In other sources the chemical property of cross-linking is also commonly ascribed to gels. *See* Sun Decl., Ex. 13 at 468 ("A gel is an extended three-dimensional, loosely cross-linked, polymer . . . ."). Accordingly, the proper construction for the term "gel" is "a three-dimensional cross-linked network."

C. "primers for co-amplifying . . . loci"
"primers for each locus"
"primers flanking the loci"

Proposed Construction: the specific primer sequences listed in the patent for each locus[6]

Construction of this term is necessary to resolve a disputed issue concerning infringement. Under the proposed construction above, the accused products do not infringe the asserted claims of the Promega patents because they amplify loci using primers having sequences different from the primer sequences found in the Promega patents.

i. The Uncertain State of the Art and Promega's Statements in the Prosecution Histories Confirm the Narrow Scope of the Claims

The terms "primers for co-amplifying . . . loci," "primers for each locus," and "primers flanking the loci" all refer to the primers used to co-amplify selected STR loci in the multiplex amplification reactions of the Promega patents. They cannot be construed to cover all possible primer sequences for any given locus.[7] Instead, these claim terms must be construed consistently with what Promega actually invented. Renishaw, 158 F.3d at 1250; Phillips, 415 F.3d at 1321.

As discussed in detail above, the state of the art with respect to multiplex amplification reactions was, by Promega's own characterization, highly unpredictable and experimental. This includes in particular the primers used in such multiplex amplification reactions. *See, e.g.*, Sun Decl., Ex. 1 at 277 ("The multiplex amplification of STR loci is extremely sensitive to different primers, thereby making primer selection critical. . . . [S]uccessful amplification and resolution

[6] The Promega Patents list specific primers corresponding to specific individual STR loci. *See* Sun Decl., Ex. 6 ('660 patent), cols. 18-19; Sun Decl., Ex. 7 ('598 patent), cols. 7-10; Sun Decl., Ex. 8 ('235 patent), cols. 12-13; Sun Decl., Ex. 9 ('771 patent), cols. 12-13.

[7] Some claims in the Promega patents include limitations which reference specific primer sequences (*e.g.*, in the '660 patent, claims 8 and 26). However, none of these claims has been asserted. The '660 and '598 patents define the term "primers" in the specifications. *See* Sun Decl., Ex. 6, col. 12, ll. 13-16; Sun Decl., Ex. 7, col. 5, ll. 57-60. The '235 and '771 patents define the term "primer." *See* Sun Decl., Ex. 8, col. 8, ll. 10-13; Sun Decl., Ex. 9, col. 8, ll. 20-23. Neither of these definitions includes any reference to particular primer sequences and would therefore be overbroad if adopted as the construction for the "primer" claim terms, as explained above.

depends largely upon primer selection."); id. at 276 ("[T]he choice of oligonucleotide primers is critical to the successful operation of multiplex amplification protocols."); id. at 305 (finding that the prior art stated "in no uncertain terms, that primer selection is a key consideration"); id. at 340. During prosecution Promega commented specifically about the uncertainty and unpredictability of designing successful primer sequences that would work in a multiplex reaction and produce clean, unambiguous results. For example:

> [T]he selection of primers and other conditions suitable for use in multiplex amplification and analysis . . . is a difficult and arduous process.
>
> [T]he selection of primers for amplifying such loci, was not a trivial matter; but, required a considerable amount of experimentation.
>
> [I]t was not possible to predict which primer pairs would work well in a multiplex amplification reaction, based upon the primers having certain properties, such as, similar annealing temperatures.

Sun Decl., Ex. 3 at 156, 159 (quoting Sprecher Declaration, ¶ 20), 177 (¶ 11); Sun Decl., Ex. 4 at 261 (¶ 6). Additional statements are listed in Appendix C, hereby incorporated fully by reference.

Co-inventor Cynthia Sprecher emphasized in her declaration that a known functional primer sequence for an individual locus could simply fail to function when used in a multiplex reaction:

> [W]e found that, while a primer pair that worked well in an amplification reaction in a "monoplex" format (i.e., in a format where only one STR locus is amplified in a single reaction, in a single container), it could fail when used in an amplification reaction in a multiplex format.

Sun Decl., Ex. 3 at 176-77 (¶ 11); Sun Decl., Ex. 4 at 260 (¶ 6). She went on to describe numerous difficulties she encountered when attempting to add primers for even a single additional locus into an existing multiplex set (*e.g.*, additional anomalous bands). Sun Decl., Ex.

3 at 177 (¶ 12); Sun Decl., Ex. 4 at 260-61 (¶ 7).[8] In fact, in arriving at the alleged inventions of the Promega patents, "***at least 65 primer pairs*** were tested for their performance in multiple STR systems during the course of identifying the functional multiplex STR loci sets claimed in the present application." Sun Decl., Ex. 3 at 176 (¶ 11) (emphasis added); Sun Decl., Ex. 4 at 260 (¶ 6) (emphasis added).

The take-away from these various accounts is, firstly, that primers were a "critical factor" to the success of a multiplex reaction. Sun Decl., Ex. 3 at 177 (¶ 12); Sun Decl., Ex. 4 at 261 (¶ 7). Yet, secondly, everything about them—their sequence, their concentration, their capability of amplifying loci without producing undesired side effects—rendered the process of identifying viable primers a "difficult and arduous process." Sun Decl., Ex. 3 at 156. Even once a viable primer for a specific locus was identified, it might have been the case that it failed to amplify the locus or produced artifacts when multiplexed with other loci. Id. at 176-77 (¶ 11); Sun Decl., Ex. 4 at 260 (¶ 6). If it did, it still might have been the case that it failed to amplify the locus or produced artifacts when multiplexed with a new and different set of loci. Id. Each new multiplex set had to be redesigned and optimized anew. Sun Decl., Ex. 1 at 308, 328. Fundamentally, according to Promega, there was no escaping the fact that a "considerable amount of experimentation" was required and success was "not possible to predict." Sun Decl., Ex. 3 at 159; id. at 177 (¶ 11); Sun Decl., Ex. 4 at 261 (¶ 6).

Given the highly unpredictable and experimental state of the art, the question must again be posed: did Promega actually invent all possible "primers for co-amplifying . . . loci," "primers for each locus," and "primers flanking the loci"? Again the answer can only be no. Promega at

[8] The specifications of all of the Promega patents also uniformly describe problems which may be encountered in designing or selecting specific primer sequences for use in multiplex reactions. *See* Sun Decl., Ex. 6 ('660 patent), col. 12, l. 66 – col. 13, l. 6; Sun Decl., Ex. 7 ('598 patent), col. 7, ll. 4-11; Sun Decl., Ex. 8 ('235 patent), ll. 25-32; Sun Decl., Ex. 9 ('771 patent), col. 11, ll. 35-42.

most identified particular primer sequences which amplified specific loci within various specific sets or groups of loci. Primer sequences other than those listed in the Promega patents for each locus are beyond scope of the alleged inventions. Therefore, the only correct construction for the terms "primers for co-amplifying . . . loci," "primers for each locus," and "primers flanking the loci" is therefore "the specific primer sequences listed in the patent for each locus."

ii. A Broad Construction of the Claims Would Exceed the Written Descriptions of the (Alleged) Inventions

The claim terms "primers for co-amplifying . . . loci," "primers for each locus," and "primers flanking the loci" are not unlimited with respect to primer sequence. For Promega to be entitled to such expansive claim scope, it must have shown that it was "in possession of the invention [as] claimed." Capon, 418 F.3d at 1357. A construction of the claims cannot "overreach" what it has actually invented, "as described in the specification." Reiffin, 214 F.3d at 1345-46. Turning again, therefore, to the specifications of the Promega patents, support is not found for the proposition that Promega generally invented all possible "primers for co-amplifying . . . loci," "primers for each locus," and "primers flanking the loci."

By the time of the '235 and '771 patents, the latest in time of the Promega patents, the specifications reveal that Promega had made little—if any—progress in identifying viable primers for use in multiplex reactions. Promega purports to describe and enable certain facets and steps involved in primer selection, but its written description merely reveals the exact same clunky, ad hoc, reiterative, and unpredictable process of trial-and-error which it had been employing since the earliest in time of the Promega patents and which was already well known and extensively lamented in the prior art. Below are a few of the alleged teachings found in the specifications of the '235 and '771 patents:

> Primers are preferably developed and selected for use in the multiplex systems of the invention by employing a re-iterative

> process . . . . Initially, this process often produces the amplified alleles in an imbalanced fashion (i.e., higher product yield for some loci than for others) and may also generate amplification products which do not represent the alleles themselves. These extra fragments may result from any number of causes . . . .

Sun Decl., Ex. 8 ('235 patent) (emphasis added), col. 11, ll. 36-46; Sun Decl., Ex. 9 ('771 patent), col. 11, ll. 46-56 (emphasis added). This is the same difficult and arduous screening process already known and described in the prior art. Further, problems with this process were also already well known, well documented, and frequently lamented in the prior art. Promega does not disclose any predictability, certainty, correlation, or trend beyond what was already known.

'235 patent	**'544 parent application**
One or more of the re-iterative selection processes described above are repeated until a complete set of primers is identified which can be used to co-amplify the at least thirteen loci selected for co-amplification as described above.	Until the actual loci are combined, primers constructed, and co-amplification attempted, it cannot be predicted, based on the teaching of [the prior art] that the combined loci can be cleanly amplified and separated.

Sun Decl., Ex. 8 ('235 patent), col. 12, ll. 25-29 (emphasis added); Sun Decl., Ex. 9 ('771 patent), col. 12, ll. 36-39 (emphasis added); Sun Decl., Ex. 1 at 308.

No shortcuts, efficiencies, or even suggestions of shortcuts or efficiencies are provided. Promega's basic advice is to "try until you get it right." This constitutes merely an invitation to endless experimentation and, moreover, only summarizes the problem without providing a solution. Indeed, this alleged teaching from the '235 patent, one of the latest in time of the Promega patents, is nearly identical to Promega's characterization of the state of the art during prosecution of the earliest in time of the Promega patents, the '544 parent application. No discernible advance in the state of the art can be found by comparing these two statements.

Together, the specifications of the Promega patents fail to teach skilled artisans to use undisclosed primers without undue experimentation. At best, the purported teachings in the '235 and '771 patent can be said to summarize what was already known in the art. The '660 and '598 patents lack even this "disclosure." Promega does not provide a solution to the problem, or mitigate or reduce in any way the extensive experimentation which would be required to practice any broader interpretation of the claims. Together, the specifications demonstrate that what Promega actually (allegedly) invented and had possession of were particular primer sequences which were found to be successful in amplifying specific loci within certain sets or groups of loci. Capon, 418 F.3d at 1357. In this case, in order for the claims to be commensurate with the scope of the alleged invention, the "primer" claim terms must be construed as "the specific primer sequences listed in the patent for each locus."

D. "multiplex amplification . . . using . . . primers"

Proposed Construction: amplifying loci together using the specific primer sequences listed in the patent

Construction of this term is necessary to resolve a disputed issue concerning infringement. Under the proposed construction above, the accused products do not infringe the asserted claims of the Promega patents because they amplify loci using primers having sequences different from the primer sequences found in the Promega patents.

Defendants propose, for the same reasons given above with respect to the claim terms "primers for co-amplifying . . . loci," "primers for each locus," and "primers flanking the loci," that the term "multiplex amplification . . . using . . . primers" should be construed to mean amplifying loci together using only the specific primer sequences listed in the patent for each locus.

E. "co-amplifying . . . loci"

Proposed Construction: when primers are used, amplifying loci together using the specific primer sequences listed in the patent

Construction of this term is necessary to resolve a disputed issue concerning infringement. Under the proposed construction above, the accused products do not infringe the asserted claims of the Promega patents because they amplify loci using primers having sequences different from the primer sequences found in the Promega patents.

The claim term "co-amplifying . . . loci" is recited as one of the steps in the method claims of the Promega patents. Defendants propose a construction for the term "co-amplifying . . . loci" to the extent that the co-amplification step is carried out using primers. For the same reasons given above for the claim terms "primers for co-amplifying . . . loci," "primers for each locus," and "primers flanking the loci," Defendants propose that the term "co-amplifying . . . loci" should be construed to include only the specific primer sequences listed in the Promega patents for each locus.

To the extent Promega may try to dispute that the "co-amplifying . . . loci" step implicates primers at all, the response is that Promega itself has already asserted that it necessarily does. First, many of the actual claims of the Promega patents explicitly recite "primers for co-amplifying" (*e.g.*, claim 25 of the '660 patent, claim 18 of the '235 patent, claim 5 of the '771 patent). Primers are therefore one of the implements necessary to carry out the co-amplifying step. (Analogously, a method reciting the step of building a house may not explicitly recite hammers and nails, but they are nonetheless necessarily implicated in the performance of the method.)

Second, Promega conceded as much during prosecution of the '235 patent when the examiner imposed a restriction requirement. Group I was drawn to "methods of determining

alleles by multiplex amplification" of a set of loci, which included the "co-amplifying . . . loci" step. Sun Decl., Ex. 4 at 205. Group II was drawn to "a kit comprising oligonucleotide primers for co-amplifying a set of" loci. Id. Promega argued:

> Applicants respectfully submit that the two groups of claims are directed to two different embodiments of the ***same invention***. The kit is designed for use in the practice of the method of the invention, while the method of the invention is preferably practiced using the kit of the invention. Applicants submit that the claims of Group I and the claims of Group II are not directed to separate and distinct inventions, but to the ***same invention***. Thus, restriction to either group of claims is improper, under 35 U.S.C. § 121.

Id. (emphasis added).

Promega unequivocally stated that its claimed method, which included the "co-amplifying . . . loci" step, was the "same invention" as the claimed kit, which included "primers for co-amplifying." Based on Promega's own characterization of its alleged invention, the "co-amplifying . . . loci" step necessarily includes primers.

V. CONCLUSION

In light of the foregoing, Defendants respectfully request the Court to adopt its proposed claim constructions.

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APPENDIX A

Statements Made by Promega During Prosecution of the Promega Patents Regarding the State of the Art

(Emphasis added except where otherwise indicated)

"[T]he identification and selection of loci suitable for multiplex analysis, prior to the present invention was a difficult task for one of ordinary skill in the art of the present invention at the time the present application was filed." Sun Decl., Ex. 2 at 227.

"[T]he selection of the specific sets of STR loci suitable for multiplex amplification and analysis requires a multitude of factors producing unobvious results." Sun Decl., Ex. 2 at 251.

"[T]he selection of primers and other conditions suitable for use in multiplex amplification and analysis, such as is claimed in claim 21, is a difficult, arduous process." Sun Decl., Ex. 3 at 156.

"It is impossible to predict from [the prior art] those loci which can be successfully co-amplified to yield unambiguous results." Sun Decl., Ex. 1 at 275.

"[T]he mere knowledge that multiplex amplification and analysis of STR loci offers several advantages over monoplex amplification and analysis of the same loci does not suggest which STR loci could be co-amplified in a particular method, such as the method of claim 21." Sun Decl., Ex. 3 at 157.

"[I]n addition to difficulties which may be encountered due to the nature of the loci themselves, multiplexing the two or more loci presently claimed in a single PCR amplification brings with it additional problems . . . . [T]hese problems are neither systematic nor predictable." Sun Decl., Ex. 1 at 271.

"Considering how many possible combinations there are of tri-, tetra-, and pentanucleotide STR loci in the human genome, and considering the anomalous band problems observed by Kimpton *et al.* '93 with the multiplex sets disclosed therein, Applicants respectfully submit that Kimpton *et al*. '93, even when viewed in combination with Caskey *et al*. and Kimpton *et al*. '94, does not teach or suggest the present claimed invention." Sun Decl., Ex. 3 at 160.

"[T]he process of identifying sets of loci which can be amplified and analyzed together is an unpredictable one, requiring a considerable amount of experimentation, even with the guidance of references . . . ." Sun Decl., Ex. 3 at 177. (Sprecher Declaration); Sun Decl., Ex. 4 at 247.

"[I]t was far from routine at the time the present invention was made to identify STR loci which were suitable for multiplex amplification and evaluation of the alleles produced thereby." Sun Decl., Ex. 3 at 178. (Sprecher Declaration); Sun Decl., Ex. 4 at 247.

"[C]riteria for avoiding loci for use in a multiplex amplification did not necessarily indicate whether a locus could be used successfully in a multiplex amplification . . . ." Sun Decl., Ex. 3 at 180. (Sprecher Declaration)

"[T]he selection of STR loci which could be amplified together was not a trivial matter, but required a considerable amount of experimentation, at the time the present invention was made." Sun Decl., Ex. 3 at 181. (Sprecher Declaration)

"Therefore, given the unpredictable nature of multiplex STR loci set selection at the time the present invention was made, the results were unpredictable, and screening was required to ensure any given set of STR loci could be amplified and evaluated together." Sun Decl., Ex. 4 at 249.

"[T]he identification of sets of STR loci suitable for co-amplification and analysis can only be accomplished after laborious screening, and the results are unpredictable." Sun Decl., Ex. 4 at 251.

"[M]any problems crop up when trying to co-amplify different loci or to increase the number of loci co-amplified in a single multiplex reaction." Sun Decl., Ex. 4 at 252.

"Some reasons for the multiplex unpredictability include: well known physical limitations of electrophoresis gels, limitations on the selection of primer combinations available for use in amplification of loci efficiently in the absence of artifacts, and the need to select sets of loci wherein the primer combinations designed for each locus do not create artifacts when the primers from one locus are combined with those of another locus." Sun Decl., Ex. 4 at 252-53.

"STR loci selection and co-amplification was shown to be a non-trivial matter and that success in these endeavors was by no means expected." Sun Decl., Ex. 4 at 253.

"[T]he selection of the specific sets of STR loci suitable for co-amplification and evaluation of the resulting mixture of amplified alleles requires taking into account a multitude of factors, which produce unpredictable results." Sun Decl., ex. 4 at 253.

"A few critical factors recognized among experts in the DNA typing field and which are used to screen for suitable STR loci, include discriminating power, absence of linkage, agreement with Hardy-Winberg equilibrium, low levels of 'shadow bands,' compatibility with other loci (for a multiplex STR system and accurate sizing of alleles. . . . These critical factors highlight the many difficulties encountered by a skilled artisans [sic] in trying to identify and select STR loci suitable for co-amplification and evaluation." Sun Decl., Ex. 4 at 253.

"Applicants take strong exception to the statement in the Official Action that the choice of STR loci to be included in a multiplex amplification reaction is arbitrary. The authors of both the primary and secondary references themselves note that there are several difficulties regarding multiplex amplifications which are presently inexplicable." Sun Decl., Ex. 1 at 274.

"The choice of loci to be included in the multiplex is not a simple matter, as shown by the difficulties encountered by the authors of the applied references." Sun Decl., Ex. 1 at 275.

"As is made clear from the references themselves, the choice of loci combinations for a successful multiplex polymerase chain reaction is far from arbitrary." Sun Decl., Ex. 1 at 301.

"[T]here are a myriad of parameters which go into a successful multiplex reaction: the choice of individual loci, the choice of primers for those loci, the combination of individual loci and primers which can be co-amplified, the balancing of template and primers to give equal output for each allele, the massive variability in the PCR cycling conditions, etc. This is by no means an exhaustive list. Moreover, the prior art simply cannot provide any indication of which parameters are critical, nor can the prior art provide any direction as to which of many possible choices is likely to be successful because the cited references admittedly do not teach the claimed loci combinations. Additionally, the applied references are replete with statements evidencing the difficulty in successfully amplifying a single STR loci [sic], much less a multiplex reaction as presently claimed." Sun Decl., Ex. 1 at 302.

"The huge number of variables, and lack of any unifying predictive theory of multiplex PCR amplification, negates the assumption that a functional multiplex can be fashioned from any arbitrary combination of loci." Sun Decl., Ex. 1 at 304.

"[T]he prior art itself notes that amplifying any given STR loci is not a given; it takes a great deal of empirical research which encompasses a huge number of experimental parameters. Further still, there is no scientific trend evidenced by the applied references which would allow one of skill in the art to predict which STR loci can be successfully amplified in combination with other STR loci, or which of the many parameters will be critical with any given combination of loci." Sun Decl., Ex. 1 at 305.

"[T]he references themselves clearly and explicitly state that the selection of loci and primers is far from arbitrary." Sun Decl., Ex. 1 at 306.

"Until the actual loci are combined, primers constructed, and co-amplification attempted, it cannot be predicted, based upon the teaching of Kimpton *et al*. and Fregeau and Fourney, that the combined loci can be cleanly amplified and separated." Sun Decl., Ex. 1 at 308.

"Simply put, different amplified loci, including STR loci, do not behave in identical or predictable fashion when subjected to PCR amplification." Sun Decl., Ex. 1 at 328.

"The references include further statements evidencing the difficulty in successfully amplifying a single STR locus, (as compared to the multiplex reactions presently claimed). Sun Decl., Ex. 1 at 334.

"PCR amplification of a single STR locus is 'highly problematic.'" Sun Decl., Ex. 1 at 335.

APPENDIX B

Statements Made By Promega Regarding the "A Set of . . . Loci"

(Emphases added except where otherwise indicated)

'544 Parent Application

- **Weber and May**
  - "Weber and May do not teach the simultaneous amplification of the pairs of STR loci now claimed in claim 1." Sun Decl., Ex. 1 at 269.
  - "Consequently, because Weber and May do not literally describe the loci to be amplified which are now positively recited in claim 1, Weber and May do not anticipate claim 1." Sun Decl., Ex. 1 at 269.
  - "Weber and May do not describe or suggest the loci which are presently recited in claim 1 (from which claim 12 depends)." Sun Decl., Ex. 1 at 277.
  - "Weber and May are completely silent regarding all of the loci currently claimed." Sun Decl., Ex. 1 at 278.
  - "Weber and May do not describe or suggest any of the loci currently claimed in claim 1, from which claim 15 indirectly depends." Sun Decl., Ex. 1 at 279.
  - "As amended, claim 1 notes the specific loci which are to be used in the method as claimed. Weber and May are completely silent regarding these loci. Moreover, due to the uncertainty of multiplex amplification protocols in general, Weber and May do not provide any guidance regarding the successful construction of a multiplex amplification protocol using the claimed loci." Sun Decl., Ex. 1 at 280.
  - Not one of the STR loci presently recited in the claims is mentioned by Weber and May." Sun Decl., Ex. 1 at 301.
  - "The most notable failure of this reference is that it does not describe the simultaneous amplification of any of the STR loci presently claimed." Sun Decl., Ex. 1 at 327.
- **Weber and May; Bassam *et al.***
  - "Weber and May do not describe any of the loci currently recited in claim 1. Bassam *et al.* are also silent regarding these loci. Consequently, a combination of Weber and May and Bassam *et al.* does not serve to render obvious claim 14 as presently amended. No teaching is contained in either of these references regarding the specific loci claimed nor do either of these references provide any guidance in constructing a

functional multiplex amplification of two or more STR loci from among those loci positively recited in the base claim." Sun Decl., Ex. 1 at 278.

- "Because the combination of Weber and May with Bassam *et al.* does not explicitly describe the presently claimed loci or provide any guidance regarding the methodology as currently claimed, Applicants submit that the rejection of claim 14 under 35 U.S.C. § 103 over Weber and May in view of Bassam *et al.* has been overcome." Sun Decl., Ex. 1 at 278

- **Weber and May; Clemens *et al.***

  - "Because neither Weber and May nor Clemens *et al.* described the presently claimed method which uses the loci recited in Fig. 1, Applicants submit that this rejection has been overcome by the above amendment." Sun Decl., Ex. 1 at 279.

  - "Neither Weber and May nor Clemens *et al.* suggest [sic] using the presently claimed loci, nor would the teaching of these two references provide any meaningful guidance regarding a multiplex amplification of these different loci." Sun Decl., Ex. 1 at 279.

- **Caskey *et al.***

  - "Caskey *et al.* do not teach these combinations of loci as claimed. Consequently, Caskey *et al.* do not anticipate claims 1 or 19 as amended." Sun Decl., Ex. 1 at 271.

  - "The Caskey *et al*. disclosure does, however describe multiplex reactions of certain defined STR loci. . . . It is important to note, however, that the teaching of these loci combinations does not serve to render obvious the presently claimed combinations of loci because the alleles of different loci migrate quite differently in gel electrophoresis. Consequently, Caskey *et al.* do not provide any relevant teaching regarding multiplexes of other loci because it is unknown from a reading of Caskey *et al.* how these different loci will behave in combination with one another." Sun Decl., Ex. 1 at 272.

  - "Because Caskey *et al*. do not describe the loci presently claimed in claims 1 and 19, and further because the teaching of a multiplex amplification of the specific alleles described in Caskey *et al*. cannot be extended to predict the success of multiplexing unrelated combinations of loci, Applicants respectfully submit that the above rejection has been overcome." Sun Decl., Ex. 1 at 272.

  - "Applicants repeat in full here the arguments made above regarding the unobvious nature of the claimed invention: 1) The invention as a whole utilizes loci combinations which are admittedly not described by Caskey *et al.*; . . . ." Sun Decl., Ex. 1 at 309.

- **Kimpton *et al*., Frégeau and Fourney**

  - "However, contrary to the assertion made in the Office Action, neither of the secondary references, Kimpton *et al.* or Frégeau and Fourney, describe the multiplex co-amplifications currently claimed in claims 4-9." Sun Decl., Ex. 1 at 273.

  - "The three multiplexes described by Kimpton *et al.* are as follows . . . . A comparison of these multiplexes with claims 4-9 as amended shows that none of the currently claimed co-amplification analyses are described by Kimpton *et al*." Sun Decl., Ex. 1 at 273-74.

  - "[N]either of these two references describe or suggest the presently claimed combinations of loci." Sun Decl., Ex. 1 at 307.

  - "Appellants note that while some of the individual loci described in these three multiplexes also appear in the appealed claims, it has been admitted that the Kimpton *et al.* reference does not teach the specific locus ***combinations*** claimed." Sun Decl., Ex. 1 at 328.

- **All prior art**

  - "Claim 30 recites a quadruplex which is specifically illustrated in Examples 23 and 26 of the specification. The simultaneous amplification and analysis of HUMCSF1PO, HUMTPOX, HUMTH01, and HUMCD4 is clearly not shown or suggested by any of the prior art now of record." Sun Decl., Ex. 1 at 282.

  - "Moreover, the prior art simply cannot provide any indication of which parameters are critical, nor can the prior art provide any direction as to which of many possible choices is likely to be successful because the cited references admittedly do not teach the claimed loci combinations." Sun Decl., Ex. 1 at 302 (emphasis in original).

  - "The combined references do not disclose or even suggest the presently claimed combinations of loci, per se, and the references clearly do not disclose or suggest that any arbitrary combination of loci can be co-amplified without undue experimentation." Sun Decl., Ex. 1 at 304.

  - "Without wishing to be overly repetetive [sic], Applicants again note that the invention as a whole utilizes loci combinations which are admittedly not described in the prior art." Sun Decl., Ex. 1 at 305.

  - "Applicants respectfully traverse this rejection for the same reasons above, and repeat here the arguments made above. First, the references do not describe the presently claimed combinations of loci." Sun Decl., Ex. 1 at 306.

  - "Appellants respectfully submit that a *prima facie* case of obviousness against the present claims has not been shown because: 1) the applied references admittedly do not describe the locus combinations presently claimed; . . . ." Sun Decl., Ex. 1 at 332.

- "It has been acknowledged that none of the STR locus combinations recited in the claims are described by the applied references." Sun Decl., Ex. 1 at 332.

- "The applied prior art simply cannot provide any indication of which parameters are critical, nor can the prior art provide any direction as to which of many possible choices is likely to be successful because 1) the references do not describe the locus combinations [in the] claims; and 2) the references clearly indicate that each individual locus responds differently when subjected to the PCR using locus-specific primers." Sun Decl., Ex. 1 at 333.

- "While not wishing to be overly repetitive, Appellants again note that the invention as a whole utilizes locus combinations which are admittedly not described in the prior art." Sun Decl., Ex. 1 at 336.

'660 Patent

- **Urquhart *et al.***

  - Claim 37 "must include three loci set forth in that claim (i.e. D7S820, D13S317, and D5S818), none of which are included in the set of loci disclosed in Urquhart et al." Sun Decl., Ex. 2 at 230-31.

  - "Applicant submits that at least three loci in each set of loci listed in the claim [25] are not disclosed by Urquhart et al. Therefore, Applicants submit that the kit of claim 25, and of claims 26-28 which are dependent thereon, are clearly not anticipated by Urquhart et al." Sun Decl., Ex. 2 at 231.

- **Kimpton-I**

  - "One of those four loci [in the multiplex disclosed by Kimpton-I] is not included in the list of loci of claim 1." Sun Decl., Ex. 2 at 232.

  - "Kimpton-I also discloses no additional short tandem repeat loci suitable for co-amplification and multiplex analysis, much less the specific sets of at least three or four loci analyzed according to the methods or using the kits of the present invention."

- **Kimpton-II**

  - Claim 25 and 27-31 "are all directed to kits designed to be used in the co-amplification of sets of loci, all of which sets include at least three STR loci not analyzed or disclosed by Kimpton-II. Therefore, Applicants submit that Kimpton-II does not anticipate any of the cited claims." Sun Decl., Ex. 2 at 233.

- **McKeowen *et al.***
  - "McKeowen et al. fails to disclose the suitability of more than two of the loci listed in claim 1." Sun Decl., Ex. 2 at 233.
  - "Furthermore, McKeowen also fails to disclose the suitability or even existence of three other loci listed in claim 1." Sun Decl., Ex. 2 at 233.
- **Oldroyd *et al.***
  - Oldroyd et al. in fact discloses experimental results obtained from co-amplifying and evaluating seven STR loci simultaneously, a set of loci which includes the loci HUMVFA31/A and HUMTH01, but which does not include any other loci included in the list of loci provided in claim 1 as originally filed." Sun Decl., Ex. 2 at 234.
  - Oldroyed et al. "fails to teach the selection of at least four loci from the group of STR loci listed in claim 1." Sun Decl., Ex. 2 at 234.
- **Oetting *et al.***
  - Applicants admit that several of the loci sets listed [in Oetting et al.] include one or two of the individual loci listed in the group of loci from which the set of loci is selected for co-amplification and evaluation according to the method of claim 1. . . . However, Applicants submit that it takes more than the disclosure of some of the individual loci in the various sets of loci co-amplified according to the present claims for any given reference to anticipate the claims." Sun Decl., Ex. 2 at 234-35.
- **Lin *et al.***
  - "[N]one of the 26 loci disclosed therein are [sic] included in the list of required loci in the lists of sets of loci analyzed according to the methods of the present claims." Sun Decl., Ex. 2 at 235.
- **Fuentes *et al.***
  - Fuentes et al. "fails to teach or suggest the specific sets of loci analyzed according to the methods of the present claims." Sun Decl., Ex. 2 at 237.
- **Bassam *et al.***
  - "Bassam et al. does not teach or suggest any method for amplifying or analyzing STR loci, much less suggest the selection of any particular set of STR loci suitable for co-amplification and analysis according to the methods or using the kits of the present invention." Sun Decl., Ex. 2 at 252.

- **Tully *et al.***
  - "Tully et al. fails to disclose . . . the sets of STR loci selected from the group of such loci provided in each cited claim." Sun Decl., Ex. 2 at 232.

- **All prior art**
  - "[T]he present invention enable[s] skilled artisans to co-amplify and analyze sets of loci not heretofore identified and disclosed as suitable for such analysis." Sun Decl., Ex. 2 at 227.
  - "[N]one of the cited references discloses the methods for selecting, co-amplifying, and evaluating the specific sets of short tandem repeat loci selected an analyzed according to the [claimed] method . . . or the [claimed] kits." Sun Decl., Ex. 2 at 229.
  - "[N]one of the three references cited by the Examiner herein teaches or suggests the selection or co-amplification of any of the sets of loci co-amplified and evaluated according to the methods of independent claims 1, 16, or 37." Sun Decl., Ex. 2 at 237.

'598 Patent

- **Frégeau *et al.***
  - "[N]either the specific sets of STR loci disclosed by Frégeau *et al.*, nor the technique of selecting STR systems for multiplex analysis disclosed therein would have suggested the method of claim 21 to one of ordinary skill in the art at the time the present invention was made." Sun Decl., Ex. 3 at 155.
  - "The Office Action admitted that Frégeau *et al*. does not specifically disclose the combinations of STR loci co-amplified and analyzed according to the present invention." Sun Decl., Ex. 3 at 156.

- **Caskey *et al.***
  - "The Office Action recognized the fact that Caskey *et al.* does not disclose any of the combinations of STR loci selected in the method claims of the present invention, or co-amplified using the kits of the present invention." Sun Decl., Ex. 3 at 158.
  - "Caskey *et al.* failed to provide any guidance which would have suggested to one of ordinary skill in the art to select any of the sets of at least three STR loci co-amplified with the methods or using the kits of the present invention." Sun Decl., Ex. 3 at 158.

- **Kimpton *et al.* '94**
  - "The Office Action recognized the Kimpton *et al.* '94, like Caskey *et al.*, did not disclose any of the combinations of STR loci selected and co-amplified according to the method or using the kit of the present invention." Sun Decl., Ex. 3 at 158.
  - "None of the sets of loci are disclosed by either Caskey *et al*. or Kimpton *et al*." Sun Decl., Ex. 3 at 159.
- **Kimpton *et al.* '93**
  - "The Office Action also noted that none of the multiplex sets disclosed by Kimpton *et al*. are the same as any of the sets of at least three STR loci co-amplified by the method or using the kits of the amended claims." Sun Decl., Ex. 3 at 159.
  - "Kimpton *et al*. '93 does not provide the guidance missing from Caskey *et al.* and Kimpton *et al.* '94, which would suggest to one of ordinary skill in the art to select a set of at least three STR loci co-amplified according to the present claimed method or kits. Sun Decl., Ex. 3 at 160.
- **Urquhart *et al.***
  - "[E]ven when Urquhart *et al.* is viewed with Caskey *et al*. and Kimpton *et al*. '94, the three references fail to suggest the selection of any of the sets of at least three STR loci co-amplified according to the method of independent method claims 21 and 40, or any of the sets of at least three STR loci co-amplified using the primers of kit claim 34." Sun Decl., Ex. 3 at 162.
- **All prior art**
  - "[T]he combined references do not suggest even a single set of STR loci co-amplified according to the methods or using the kits of the present claims." Sun Decl., Ex. 3 at 164.

Sprecher Declaration (Submitted During Prosecution of the '598 and '235 Patents)

- "Neither of the specific sets of three STR loci disclosed by Frégeau *et al.* as being suitable for multiplex amplification are included in the sets of loci listed in claim 21 after amendment." Sun Decl., Ex. 3 at 176, ¶ 10.
- "Furthermore, no more than two of the STR loci disclosed in the reference (e.g., Table 2 of Frégeau *et al.*) are included in any of the sets of at least three loci listed in step (b) of claim 21 as amended." Sun Decl., Ex. 3 at 176, ¶ 10.

- "None of the multiplex sets of loci described in Caskey *et al.* are included in the set of at least three STR loci in any of the rejected independent claims, as amended herein." Sun Decl., Ex. 3 at 179, ¶ 17.

- "This set of four STR loci [disclosed in Kimpton *et al.* '94] is not one of the sets of at least three loci selected for co-amplification in the methods or using the kits of the present invention." Sun Decl., Ex. 3 at 8, ¶ 19.

- "Specifically, none of the three cited references disclose any of the sets of at least three STR loci that can be amplified together, which are selected in a step of each of the method claims and that are co-amplified using the kits of the present invention." Sun Decl., Ex. 3 at 181, ¶ 20.

- "The Office Action also notes, correctly, that 'the combinations of loci [disclosed in the prior art] are not identical to the combinations claimed.' (Office Action, p. 13). As noted above, neither Caskey *et al.* nor Kimpton *et al.* '94 teach [sic] the sets of at least three STR loci of the present claims, after amendment, as well. Therefore, even when the three references are viewed together, none of the sets of loci amplified using the methods or kits of the present invention are taught." Sun Decl., Ex. 3 at 181, ¶ 21.

- "None of the sets of at least three STR loci listed in any of the present pending independent claims are included within the quadriplex disclosed by Urquhart *et al*." Sun Decl., Ex. 3 at 183, ¶ 23.

'235 Patent

- **Lin *et al.***

  - "Lin *et al*. does not teach the selection of even a single short tandem repeat locus, much less the selection of the above listed thirteen loci." Sun Decl., Ex. 4 at 246.

- **Caskey *et al.***

  - "Caskey *et al.* failed to provide any guidance which would have suggested to one of ordinary skill in the art to select any of the sets of at least three STR loci co-amplified with the methods or using the kits of the present invention." Sun Decl., Ex. 4 at 251.

- **All prior art**

  - "Specifically, Applicants argue that none of the three references, whether viewed separately or together, teach or suggest any kit for multiplex amplification of at least thirteen STR loci." Sun Decl., Ex. 4 at 255.

APPENDIX C

Statements Made By Promega Regarding "Primers"

(Emphases added except where otherwise indicated)

"[T]he selection of primers and other conditions suitable for use in multiplex amplification and analysis . . . is a difficult and arduous process." Sun Decl., Ex. 3 at 156.

"[T]he selection of STR loci which could be co-amplified, and the selection of primers for amplifying such loci, "was not a trivial matter; but, required a considerable amount of experimentation." Sun Decl., Ex. 3 at 159 (quoting Sprecher Declaration, ¶ 20).

"[I]t was not possible to predict which primer pairs would work well in a multiplex amplification reaction, based upon the primers having certain properties, such as, similar annealing temperatures." Sun Decl., Ex. 3 at 177, ¶ 11; Sun Decl., Ex. 4 at 261, ¶ 6.

"'[T]he primers to be used in the method as claimed, or to be included in the kit as claimed, are critical to the operation of the claimed invention. These primers are not described in the prior art, nor can they be deduced from the prior art minus a vast amount of experimentation." Sun Decl., Ex. 1 at 341.

"[O]nly a limited number of primers could be designed for each individual locus while providing efficient amplification and generating appropriate product in the absence of artifacts." Sun Decl., Ex. 4 at 253.

"[T]here was a need for primer designs which did not create artifacts from the combination of primers from one locus with those of another locus (thus limiting the number of possible selections for multiplex primer design." Sun Decl., Ex. 4 at 253.

"[T]he disclosure of a few primers which happen to work well in one multiplex or in multiple monoplex reactions would not have suggested the present claimed invention to one of ordinary skill in the art at the time the present invention was made . . . ." Sun Decl., Ex. 3 at 161.

CERTIFICATE OF SERVICE

I certify that on March 30, 2011, I electronically filed the above with the Clerk of Court, United States District Court for the Western District of Wisconsin through the Court's ECF system, which will send notice via electronic filing to all counsel of record.

By: /s/ Marilou S. Roxas

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